Research Article

Bone changes in the lower limbs from participation in an FES rowing exercise program implemented within two years after traumatic spinal cord injury

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Objective: To determine the effect of a functional electrical stimulation (FES) rowing program on bone mineral density (BMD) when implemented within two years after SCI.
Design: Prospective.
Setting: Health Care Facility.
Participants: Convenience sample; four adults with recent (<2 years) traumatic, motor complete SCI (C7-T12 AIS A-B).
Intervention: A 90-session FES rowing exercise program; participants attended 30-minute FES training sessions approximately three times each week for the duration of their participation.
Outcome Measures: BMD in the distal femur and tibia were measured using peripheral Quantitative Computed Tomography (pQCT) at enrollment (T_0) and after 30 (T_1), 60 (T_2), and 90 (T_3) sessions. Bone stimulus was calculated for each rower at each time point using the average number of weekly loading cycles, peak foot reaction force, and bone mineral content from the previous time point. A regression analysis was used to determine the relationship between calculated bone stimulus and change in femoral trabecular BMD between time points.
Results: Trabecular BMD in the femur and tibia decreased for all participants in $T_{0\text{-}1}$, but the rate of loss slowed or reversed between $T_{1\text{-}2}$, with little-to-no bone loss for most participants during $T_{2\text{-}3}$. The calculated bone stimulus was significantly correlated with change in femoral trabecular BMD ($P = 0.016$; $R^2 = 0.458$).
Conclusion: Consistent participation in an FES rowing program provides sufficient forces and loading cycles to reduce or reverse expected bone loss at the distal femur and tibia, at least temporarily, in some individuals within two years after SCI.
Trial Registration: NCT02008149.

Keywords: Spinal cord injury, Paralysis, Functional electrical stimulation, Bone density, Rowing, pQCT, FES rowing, SCI, FES

Introduction

Substantial bone loss and increased fracture risk in the lower limbs are well-known secondary complications of spinal cord injury (SCI) affecting nearly all individuals with motor complete SCI. Within three years after SCI, bone density in the distal femur is nearly 50% lower than that of a sex-matched able-bodied

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reference group.[1] This marked decrease in bone density results in a high incidence of low-trauma fracture for individuals with SCI.[2,3] The most common sites of fracture are around the knee (distal femur and proximal tibia) and above the ankle (distal tibia).[4,5] Post-SCI fragility fractures often result in complications, substantial medical costs, prolonged hospital stays and considerable morbidity.[6,7] Yet, despite much research, a consistently reliable treatment option has not been identified.

Pharmacological interventions have shown disappointing results in the SCI population, particularly in the areas at greatest risk for fracture.[8–11] Post-SCI bone loss is largely a function of disuse due to the total loss of voluntary muscle-induced lower limb forces after motor complete SCI. It is thought that by restoring those forces in some way, post-SCI bone loss could be attenuated or prevented. Most evidence suggests that static weight-bearing is generally ineffective at preserving bone after SCI.[12] However, functional electrical stimulation (FES) has shown some promise in attenuating post-SCI bone loss. In one study, subjects participating in standing frame therapy augmented by a “high-dose” of isometric quadriceps stimulation had a slower rate of bone loss in the distal femur compared to individuals in the “low-dose” or “no-dose” groups.[13] Some studies investigating FES cycling have reported improvements in bone density at the distal femur[14,15] and proximal tibia,[16] yet several studies in recent reviews reported no improvement.[11,12]

FES rowing was developed in the early 1990s as an aerobic training paradigm for individuals with SCI.[17–20] FES rowing takes advantage of coordinated voluntary upper body exercise in combination with electrical stimulation of the large muscle groups in the legs to produce a near-full-body exercise. Previous studies have demonstrated the positive effects of FES rowing on cardiovascular and respiratory health in individuals with SCI.[19,21–23] Three case studies of single individuals and one study involving a small cohort have also shown that FES rowing may benefit bone health in those with SCI > 2 years.[24–27] However, no investigations have targeted the effects of FES rowing on bone health early after SCI when bone mass decreases most rapidly. The purpose of this study was to determine whether an FES rowing exercise program can reduce or reverse expected post-SCI bone loss when implemented within two years after injury in a case series of four individuals.

Methods

Study design and participants

All study procedures were approved by the Stanford University Institutional Review Board and informed consent for participation and use of data were obtained from each participant prior to involvement in research activities.

We enrolled four participants with traumatic, motor complete spinal cord injury, C7-T12, AIS A or B, who were 3–24 months post-SCI. Additional inclusion criteria were physician’s clearance to exercise; 18-years or older; ability to perform safe, independent transfers; sufficient passive hip, knee, and ankle range of motion to perform rowing; and responsiveness to muscle stimulation of the quadriceps and hamstrings without uncontrolled symptoms of autonomic dysreflexia. Exclusion criteria were pregnancy, lower limb fracture since SCI, additional medical conditions known to impact bone metabolism (e.g. renal disease), use of medications affecting bone density (e.g. bisphosphonates), additional neurological disease, implanted electronic devices (e.g. pacemaker), current thrombosis, coronary artery disease, and family history of sudden cardiac death. Participant characteristics are provided in Table 1.

Intervention

The exercise intervention program involved participation in 90 FES sessions at our laboratory over a 9- to 12-month period. Each session lasted 30–60 min with up to 30 min of active training time.

Muscle conditioning

Prior to performing FES rowing, participants completed a muscle conditioning program to develop sufficient strength and endurance in the quadriceps and hamstrings. The conditioning program consisted of seated FES leg extension/flexion. FES was delivered to the quadriceps and hamstrings via self-adhesive surface electrodes (Pals Platinum; Axelgaard Manufacturing Company Ltd, Fallbrook, CA) connected to a four-channel electrical stimulator (Odstock O4CHS; Odstock Medical Ltd., Salisbury, UK). Participants remained seated in their wheelchairs with pillows placed behind their legs. FES (40 Hz, 450 μs)

Table 1 Participant characteristics.

Subject	Age (years)	Sex	Time post-SCI (months)	Injury level	AIS[a]	Mass (Kg)	Total time enrolled (months)
1	43	M	16	T4	A	87	12
2	35	M	11	T10	A	90	9
3	29	M	13	T2	B	101	10
4	23	M	10	C7	B	62	9

[a]American Spinal Injury Association (ASIA) Impairment Scale. A = Complete: No sensory or motor function, B = Sensory incomplete: sensory but not motor function is preserved below the neurological level.

was supplied simultaneously to the quadriceps of one limb and the hamstrings of the contralateral limb for five seconds followed by a one-second rest; the pattern was then repeated for the opposite limb. This produced an alternating concentric quadriceps kick-and-hold while the opposing limb flexed at the knee with an isometric hamstring contraction. Stimulation amplitude (0–120 mA) varied and was adjusted throughout each session in order for the quadriceps to produce full knee extension and for the hamstrings to produce visible knee flexion against the pillows. When the participant was able to perform 30 min of FES muscle conditioning, maintaining full knee extension throughout, he progressed to FES rowing. The muscle conditioning program varied between participants, lasting from two to eight weeks.

FES rowing

FES rowing was performed using a Concept2 Model D ergometer (Concept2, Morrisville, VT) with adapted components (Paddlesport Training Systems, East Hardwick, VT) which provided trunk stability and prevented lateral leg movement (Fig. 1). The Odstock O4CHS stimulator was used to provide bilateral stimulation to the quadriceps and hamstrings. Stimulation timing was controlled manually by the participant using a push-button-switch attached to the ergometer handle; pushing the button activated the quadriceps, releasing the button activated the hamstrings. The technique for FES rowing used by our research group follows that of able-bodied rowing; that is, leg extension is followed by arm pull (video available in supplemental material). Participants were instructed to keep their arms fully extended during early leg extension and to flex their arms only as the legs reached mid- to near-full extension. FES rowing sessions began with short intervals (1–3 min) and progressed until participants could perform 30 min of continuous FES rowing with occasional short breaks for hydration.

Bone measurements

Bone measurements of the distal femur and distal tibia were performed using peripheral Quantitative Computed Tomography (pQCT) (XCT3000, Stratec Medizintechnik, Pforzheim, Germany). Scans were obtained at four time points in the study: at enrollment (T_0), and after 30 (T_1), 60 (T_2) and 90 (T_3) exercise sessions. The left leg was scanned unless previous fracture (within the last 10 years) or the presence of hardware prevented scanning the ankle and knee of the same leg; then the right leg was scanned. Scans were obtained using methods described previously by Eser *et al.*[1] Scout views of the distal femur and tibia were obtained to place a reference line at the distal end of each bone. Cross-sectional scans were then performed in the distal epiphyses of the femur and tibia at 4% of bone length with a slice thickness of 2.2 mm. Tibia scans were obtained with the standard procedures provided by the manufacturer using a voxel size of 0.5 mm edge length. Femur scans were obtained with a voxel edge length of 0.3 mm because of the very thin femoral cortical shell.

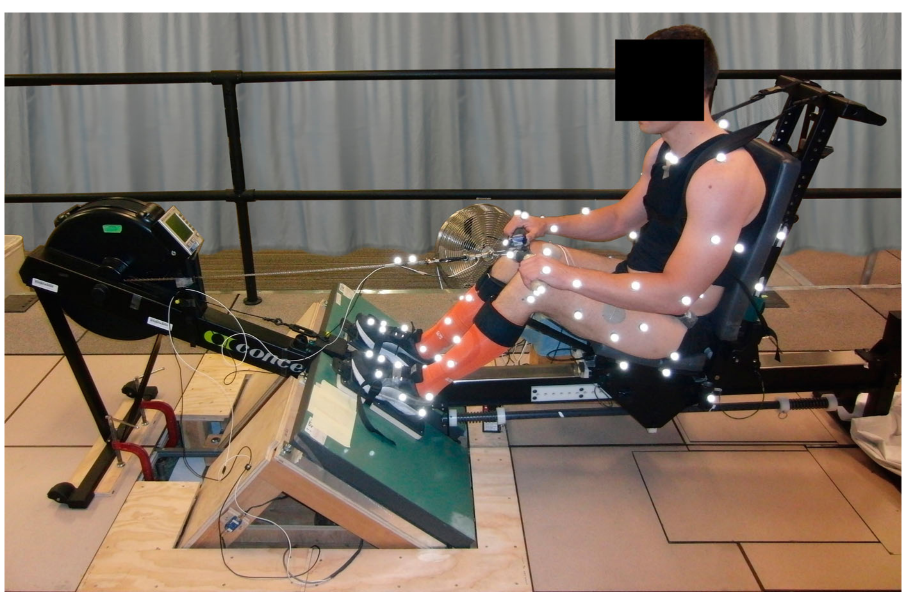

Figure 1 A participant with SCI on the adapted FES rowing ergometer during a force collection session. Foot stretchers were removed from the ergometer frame and angle-mounted force plates were used to measure the foot-contact forces produced during FES rowing.

We used software provided by the manufacturer (XCT 6.00B, Stratec Medizintechnik, Pforzheim, Germany) to calculate bone mineral content (BMC), total bone mineral density (BMD) and trabecular BMD at each site. The periosteal surface was identified using a built-in contour algorithm (C31) designed for sites with a thin cortical shell and using thresholds of 181 mg/cm^3 for the tibia and 149 mg/cm^3 for the femur. Trabecular BMD was calculated as the mean density of the central 45% of the total cross-sectional area using a standard concentric peel (P1) for the tibia and a concentric peel with allowance for concave surfaces (P11) for the femur. All scans were filtered using a manufacturer provided and recommended filter C04, which applied a 3×3 filter to all voxels, followed by a 5×5 filter to voxels with density between –500 and 600 mg/cm^3.

Force and loading cycles

At three time points (T_1, T_2, T_3), six-degree-of-freedom forces were recorded separately under each foot using two force plates (Bertec Corp., Columbus, OH) while the subject actively rowed during an FES rowing training session. The foot-stretchers were removed from the ergometer and foot-stretcher-covers were affixed to the surface of the two force plates. The force plates were mounted on custom support structures that were bolted to the concrete floor; the ergometer was positioned so that the force plates replicated the angle and position of the ergometer foot-stretchers. The participant's feet were then strapped directly to the force plates for force measurement tests (Fig. 1). Participants warmed up for approximately five minutes, after which, forces were recorded at 960 Hz for 20 s while rowing continued. Five consecutive rowing strokes (beginning and ending with the participant at the catch, or forward-most, position) were selected for further analysis. The peak foot reaction force that occurred during each stroke was calculated and averaged over five trials. Forces were not measured at time T_0 because participants did not have sufficient strength to perform FES rowing until they had completed several weeks of muscle conditioning.

The number of lower limb loading cycles from each FES rowing session was determined using an accelerometer (GT3X+, ActiGraph Corp, Pensacola, FL) attached to the seat of the rowing ergometer. The average number of weekly loading cycles between measurement time points (i.e. $T_{0\text{-}1}$, $T_{1\text{-}2}$, and $T_{2\text{-}3}$) was calculated.

Bone stimulus calculation

We computed a single metric for the bone stimulus which accounts for both the magnitude of force and the number of loading cycles. Based on concepts described by Carter *et al.*,[28] bone stimulus was defined as:

$$\text{Bone Stimulus} = \left[n* \left(\frac{F}{BMC_0} \right)^{m} \right]^{(1/2m)} \quad (1)$$

where n is the average number of weekly loading cycles since the previous time point, F is the average peak foot reaction force in Newtons in the limb of interest, and BMC_0 is bone mineral content in milligrams in the distal femur from the previous time point. The exponent m is an empirically determined constant that accounts for the relative importance of force magnitude and loading cycles in bone modulation. The exact value for m may vary by application, but has been determined previously to have a minimum value of 2, indicating that the magnitude of the force has a greater influence on bone density than does the number of loading cycles.[29] Integer values of m between 2 and 6 were tested in a post-hoc analysis, as has been done previously,[29–32] to determine which value produced the highest correlation between bone stimulus and the change in bone density at the distal femur. In the present study, we found that m = 2 produced the highest correlation.

Statistical analysis

Regression analysis was used to determine the relationship between the calculated bone stimulus and change in femoral trabecular BMD between time points. We also used an exploratory regression analysis to determine the relationship between the change in femoral trabecular bone density and the average number of weekly FES exercise sessions attended. Regression analyses were performed in Excel (Microsoft Office Professional Plus 2010, Microsoft Corporation, Redmond, WA).

Results

Participants

All four individuals completed all 90 FES exercise sessions, three force capture sessions, and four bone density scans. Participant compliance to the schedule of three weekly exercise sessions dictated the total duration of involvement, which varied from 9 to 12 months. Participants averaged attendance at 2.4 weekly sessions; total participation times can be seen in Table 1. All subjects in our study tolerated the program well and reported enjoying the training. No serious adverse events were encountered. Three participants experienced mild autonomic dysreflexia (AD) with initial exposure to FES. AD decreased with FES exposure while participants' blood pressure was closely monitored. Three participants also experienced mild shoulder discomfort. Shoulder discomfort was treated by resting from FES rowing for a few days or by adjusting the participant's arm position during handle pull. All participants returned to normal, discomfort-free rowing.

Bone density

Femur

Trabecular bone density (BMD_{Trab}) in the distal femur decreased for all participants between T_0 and T_1 (range: –5% to –11% of baseline), (Fig. 2, top). Between T_1 and T_2, two participants experienced a substantially decreased rate of loss in BMD_{Trab} (from –7% to –3% and from –5% to 0%) and the remaining two participants demonstrated an increase in BMD_{Trab} during this time period (+6% and +8%). From T_2-T_3, three participants experienced little or no trabecular bone loss in the distal femur (range: –1% to +2%). The fourth participant experienced a return of bone loss (–10%).

Tibia

Distal tibia trabecular bone followed a similar pattern to femoral trabecular bone, with losses from T_{0-1}, a decreased rate of loss for most participants from T_{1-2} and little to no loss from T_{2-3} (Fig. 2, bottom).

Bone stimulus

The bone stimulus was significantly correlated with change in BMD in the femur ($P = 0.017$; $R^2 = 0.452$) (Fig. 3). The average number of loading cycles per week varied among subjects and also within subjects (between time points) throughout the exercise program (range: 902–2146 cycles per week) (Table 2). Peak foot reaction forces varied between 18% and 26% of participants' bodyweight (Table 3). The average number of weekly training sessions attended was also significantly correlated with the change in BMD in the distal femur ($P < 0.001$; $R^2 = 0.700$) (Fig. 4).

Discussion

The results of this study provide evidence that an FES rowing exercise program can reduce or reverse the expected rate of bone loss, at least temporarily, within the first few years after SCI. With consistent FES rowing, participants in this study experienced a deviation from the exponential curve of post-SCI bone loss determined by Eser *et al.*[1] Only one participant experienced a return to substantial bone loss during T_{2-3}. It is important to highlight that bone is constantly remodeling in response to the regular pattern of applied forces. Because of this, an extended break in training likely caused a return to the rapid rate of bone loss experienced prior to engaging in FES rowing. This was likely the case for Subject 1 who had 20- and 19-day breaks in training during T_{0-1} andT_{2-3} respectively, and experienced substantial bone loss during both of these time windows (–11% T_{0-1} and –10% T_{2-3}). No other participants experienced such extended breaks in training.

Positive effects on bone in response to FES rowing have been previously reported in three case study publications of two individuals with SCI >2 years.[24–26] Gibbons *et al.* reported bone parameters of one individual with SCI (male, T4, AIS A, >13 years post-injury) who had been FES rowing approximately three times per week for >8 years. Using dual energy x-ray absorptiometry (DXA), pQCT,[26] and high-resolution pQCT,[25] they identified superior bone parameters in the FES rower compared to age-matched individuals with SCI who were not FES trained. They also identified that several trabecular and cortical microstructural parameters of the FES rower were comparable to age-matched, able-bodied individuals. Deley at al. observed a 19.4% increase in femoral neck BMD as measured by DXA in response to a thrice weekly, 9-month FES rowing intervention in one individual with SCI (female, T4-5, AIS A, 2 years post-SCI).[24] While those studies suggest promise for FES rowing in individuals with SCI greater than two years, the present study provides support for the use of FES rowing early after injury to preserve bone mass before it is lost.

To our knowledge, only one study has reported an FES rowing intervention that had no effect on BMD.[33] In that study, the primary outcome measures were related to shoulder pain; total body DXA scans were performed to determine body composition before and after six-weeks of FES rowing. It is not surprising that significant bone change was not observed; a six-week intervention is very brief considering the time required for osteoid deposition and bone mineralization. Further, total body scans have lower resolution than regional scans and do not provide high-fidelity information about localized changes in the lower limbs. We do not believe that these negative results provide evidence of an inability of FES rowing to preserve bone health, but rather that the intervention and outcome measures were not designed with intent to study bone density changes.

In our study, participants who attended an average of two or fewer weekly 30-minute FES exercise sessions over a given time window (e.g. T1-2, T2-3, etc.)

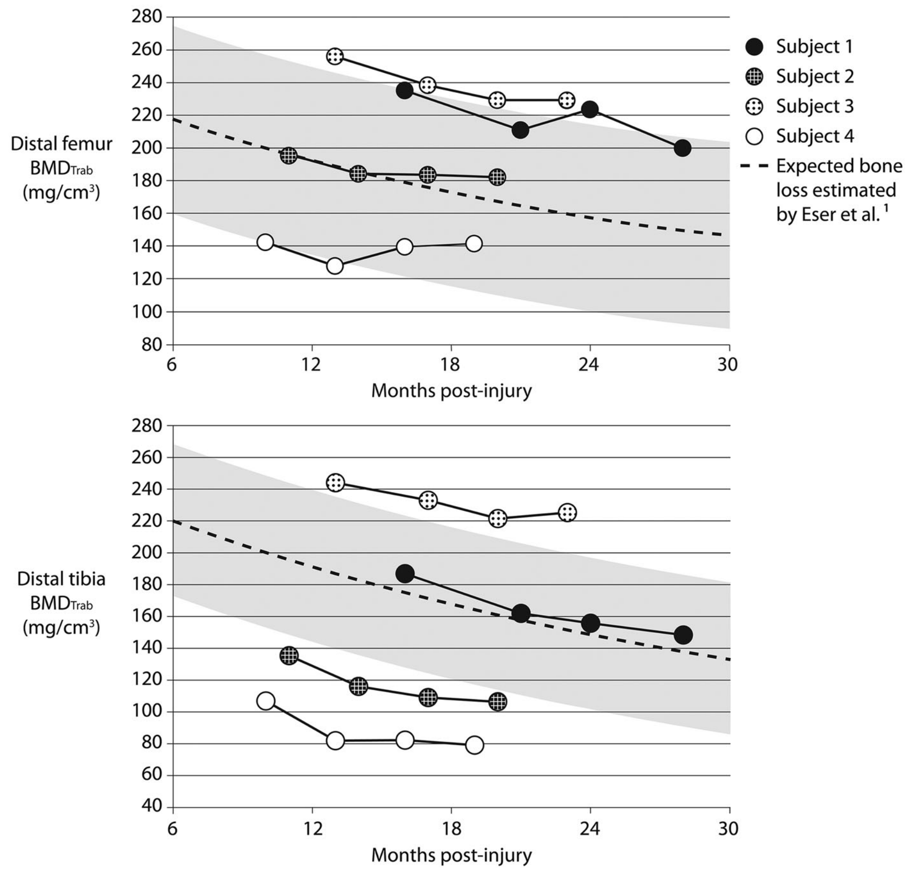

Figure 2 Trabecular bone mineral density (BMD_{Trab}) from pQCT scans in the distal femur (top) and distal tibia (bottom) over time post-SCI with involvement in the FES rowing exercise intervention. Participants attended 30 sessions between each measurement time point. Expected bone loss[1] is shown in the dotted line with ±2 standard deviations indicated by the shaded gray area.

continued to experience bone loss in the distal femur (Fig. 4). However, when the average number of weekly sessions was 2.5 or 3, the rate of bone loss was generally stopped or reversed. Similar dose-dependent responses to FES cycling and FES rowing have also been shown previously.[11,27,34] However, the average weekly number of sessions attended does not account for differences in the magnitude of foot forces or the number of loading

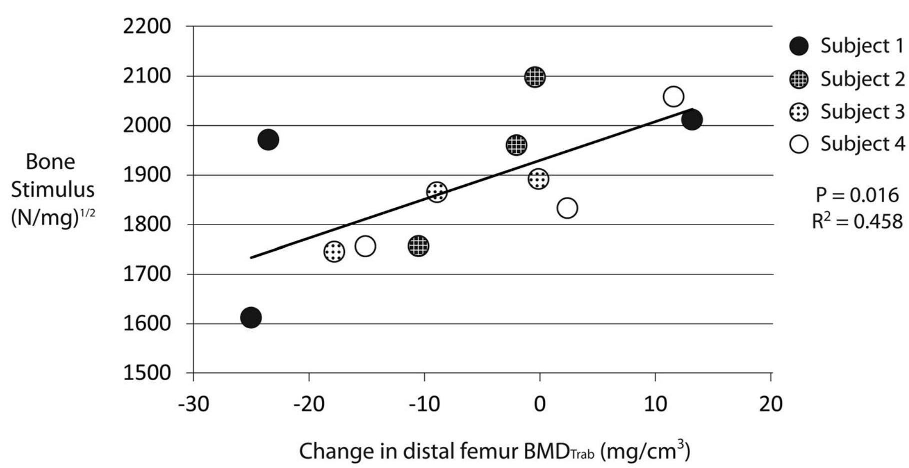

Figure 3 Bone stimulus, which was calculated using the average number of weekly loading cycles between time points, the average peak foot reaction force (N), and bone mineral content (mg) from the previous time point, was significantly correlated with the change in bone density in the distal femur between time points.

Table 2 Average weekly loading cycles between exercise sessions 0–30 (T_{0-1}), 31–60 (T_{1-2}), and 61–90 (T_{2-3}).

Subject	T_{0-1}	T_{1-2}	T_{2-3}
1	902	1786	1445
2	1035	1574	1726
3	1474	1718	2146
4	1661	1887	1981

cycles applied during each session, both of which play a key role in bone remodeling and could substantially influence study results.

Importance of collecting and reporting a measure of bone stimulus

The significant relationship between bone stimulus and BMD supports the importance of reporting both force magnitude and the number of loading cycles or a single measure that accounts for both. Because bone maintenance is a response to the magnitude of force and the number of loading cycles, it is critical to know these values in order to effectively interpret the results of studies investigating therapeutic interventions for bone health. Even within FES rowing, two participants may be exposed to very different bone stimuli due to differences in the rowing technique (affecting the magnitude of forces) or adherence to the training schedule (affecting the number of loading cycles). Reporting the bone stimulus or a similar quantification of force and loading cycles could help elucidate the mixed results seen in response to therapeutic interventions and would allow for easy comparison between different exercise interventions (e.g. FES rowing versus FES cycling).

Limitations

We acknowledge that there are several limitations to this investigation. The primary limitation is the small number of subjects involved; however, our findings provide an encouraging foundation suggesting that additional work is warranted. We also acknowledge that it would have been ideal to compare results to an age- and injury-matched control population; however, historical data from Eser *et al.*[1] allowed us to explore the effects of FES rowing on bone loss despite the lack of a control group in this study.

Defining the FES rowing intervention by number of sessions rather than calendar time may also be considered a limitation; however, we believe that this was appropriate and reasonable for this population given potential barriers such as mobility or other issues that might interfere with attendance. The intent in this design was for the 90-sesson program to reflect 9 months of thrice weekly FES exercise sessions with approximately 85% compliance. However, some participants maintained a lower compliance, thus taking more than 9 months to complete the program (Table 1). This was accounted for by comparing our results to expected bone loss using months-post-injury rather than binning results based on the measurement time point. Extended breaks in training, such as those experienced by Subject 1, would have negatively affected bone density regardless of whether the intervention was defined by calendar months or by the number of sessions. In our study, a break in training increased the calendar time between measurements, while in a calendar-based intervention, a similar break would have been reflected by low compliance. Adherence to the thrice weekly training schedule may have been negatively influenced by the requirement to attend FES rowing sessions at our facilities. In two previous case studies the participant had access to home-based FES rowing and performed FES muscle conditioning on non-rowing days.[25,26] Participants in the present study did not have access to home-based FES rowing or to FES for muscle conditioning on non-rowing days. It is reasonable to speculate that home-based access or continued FES muscle conditioning may have improved compliance and/or contributed to a greater benefit to bone health than we observed.

Finally, we acknowledge that foot reaction force magnitudes of less than one-quarter of bodyweight are small compared to the forces experienced by non-SCI individuals during everyday weight-bearing activities. However, despite these relatively low forces, we observed a positive bone response to the FES rowing program. It is important to note that foot forces are not equivalent to the forces experienced by the bones. Muscles, ligaments, and other structures within the joints, bone geometry and the joint angles experienced during FES rowing all contribute to the complex internal forces acting on the bones. We believe that using more accurate internal skeletal loading in the bone stimulus equation would produce a higher correlation between the bone stimulus and the change in BMD between time points.

Table 3 Average peak foot reaction force as a percentage of body weight (%BW) measured after 30 (T_1), 60 (T_2), and 90 (T_3) FES sessions.

	Foot force (%BW)		
Subject	T_1	T_2	T_3
1	23	24	26
2	19	21	18
3	18	19	17
4	18	22	18

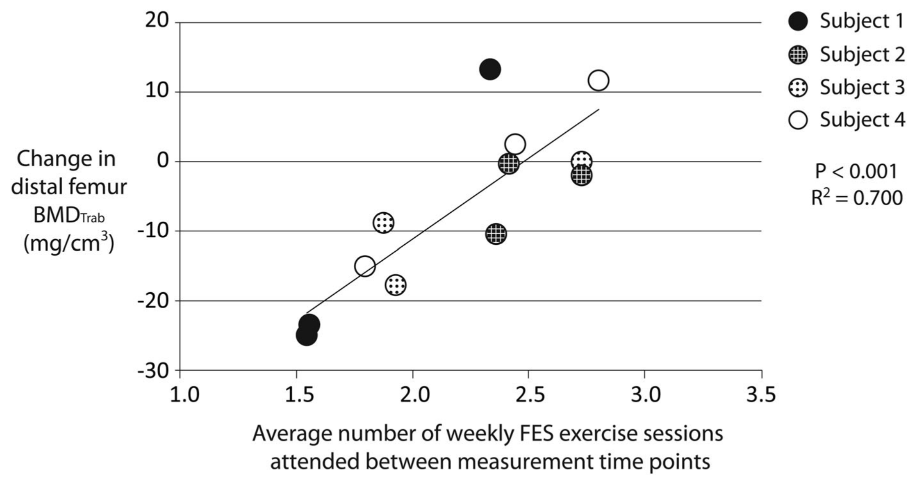

Figure 4 The average number of weekly FES training sessions attended between time points was significantly correlated with the change in trabecular bone mineral density in the distal femur since the previous time point.

However, calculation of such forces requires sophisticated simulations of human movement and is beyond the scope of the present study. Because FES rowing involves stimulating muscles which span the knee, we expect that the forces acting on the distal femur in particular are much higher than the measured foot reaction forces. Musculoskeletal models can be used to estimate muscle and joint reaction forces during activity; future work should look at the relationship between calculated knee reaction forces and changes in BMD.

Conclusion

In conclusion, consistent participation in an FES rowing exercise program appears to cause a deviation from expected bone loss within the first few years after SCI in some individuals. In this study, all four participants experienced at least one segment of time during the FES rowing intervention in which very little or no bone was lost in the distal femur. We believe that these results add to previous work building the case to further investigate FES rowing for the purposes of benefitting bone health after SCI.

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Disclaimer statements

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Conflicts of interest The authors report no conflicts of interest.

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